

## A Case Series on Tramadol Induced-Seizures

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**ABSTRACT**

Tramadol is a synthetic analogue of codeine which has been in the market since 1995. It is a racemic mixture in which the each of the enantiomer is responsible for each of its dual analgesic mechanism. The seizure inducing effect of tramadol is widely studied and reported. The tramadol can provoke seizure in patients with epilepsy and those with no history of epilepsy even with the recommended doses. The other precipitating factors are excessive doses or co-administration with other seizure inducing drugs.

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[sree.dhevachandra@gmail.com](mailto:sree.dhevachandra@gmail.com)**Funding:** Nil**Competing Interests:** Nil**Keywords:** Tramadol, epilepsy, opioid agonist, proconvulsant effect, analgesics**INTRODUCTION:**

Opioids have been the mainstay of pain treatment for thousands of years and they remain so today. The first discovered opioid analgesic is Morphine (1806) followed by Codeine (1832) and Papaverine (1848).(1) Even though they were remarked as "God's own medicines" because of their remarkable beneficial effects, they are well known for their toxic side effects and additive potential. These practical difficulties have lead to the discovery of synthetic opioids in which tramadol is the most widely used one. Unfortunately these synthetic opiates too possess some of the liabilities of the natural opiates. Tramadol is a synthetic analogue of codeine which is discovered in 1970s. The US FDA approved tramadol in March 1995. It acts as a pure opioid agonist and is indicated for moderate to severe pain. It works by agonism at the  $\mu$ -opioid receptor. Studies proves that the effects of tramadol is not fully antagonised by naloxone(2) and it shows another important mechanism of tramadol which is the reuptake inhibition of monoamines which results in activation of descending inhibitory system in CNS.(3,4,5) Tramadol is a racemic mixture in which the each of the enantiomer is responsible for each of the dual analgesic mechanism. (6,7)

The peak plasma levels of tramadol occurs at about 1.5 hours after intake, it crosses blood brain barrier and plasma elimination half-life is 5-6 hours. Most excretion takes place through the kidneys. Elimination half life of tramadol is 5-6 hours. Therapeutic blood levels in adults are about 100-300 ng/ml (0.1- 0.2  $\mu$ g/ml). (8) The maximum recommended dose is 400 mg/day. (9) Nausea,

vomiting, dizziness, dry mouth, sedation, and headache are the common adverse effects associated with tramadol. Respiratory depression induced by tramadol is less when compared with equianalgesic doses of morphine.(10) The seizure inducing effect of tramadol is a widely studied one. One study reported tramadol have an anticonvulsant effect in mice.(11) There are many studies reporting proconvulsant effect of tramadol in humans. (12-15)

**CASE 1:** A 24 year old male patient was admitted in the surgery ward with complains of bleeding per rectum. The colonoscopy revealed internal haemorrhoid and he was recommended for surgery (haemorrhoidectomy) . This patient had no past history of seizure, DM, HTN. As preoperative medication, he was given inj. ceftriaxone, inj. Pan, Inj. Tramadol inj. ondansetron. Surgery done and the next day inj tramadol was given, within few minutes he developed 1 episode of seizure GTCS (generalised tonic clonic seizures) which lasted for 1-2 minutes. Drug (inj. Tramadol) was withdrawn from medication chart, while other drugs continued and aceclofenac was added to regimen. Antiepileptics were not included in the treatment plan. No further episodes of seizure was reported after withdrawing tramadol from the regime. Patient became better and discharged in 5 days.

**CASE 2:** A 31 year old male patient was admitted in department of surgery with complaints of abdominal pain, burning sensation, headache and nausea. He had no history of fever, any drug intake, seizure. USG showed hepatomegally with moderate fatty changes

and he was diagnosed as gastritis and given Injection Pan, Buscopan and Tramadol. Patient developed an episode of seizure on third day of admission. oxygen inhalation was given to patient as oxygen saturation decreased and no antiepileptics given. Injection Tramadol was withdrawn and Diclofenac sodium added to the regimen. Patient discharged after 6 days.

**CASE 3:** A 34 year old female was admitted with complaints of pain at right lower abdomen, one episode of vomiting. she had similar complaints one week before and has done conservative management for acute appendicitis, appendectomy was done. Injection tramadol 50mg was given for post operative pain management and within 24 hours she developed convulsions and nausea. It was also diagnosed as a GTCS type seizure. The suspected drug tramadol was excluded from the treatment plan and for pain relief injection diclofenac 75mg/1ml was given instead of tramadol. Injection ondansetron relieved nausea. She was discharged in 6 days.

**Discussion:** In these three cases other causes of seizures like history of epilepsy, head trauma, metabolic reasons, drug interactions etc were inspected but nothing found positive. No antiepileptics were given for management of seizures. They had only one seizure episode of GTCS type which relieved on withdrawal of the drug tramadol. So many studies are there reporting seizures associated with high dose of tramadol.(16,17) Here in these cases the dose of tramadol is within the normal level and similar reports are seen with some researches.(18-21) Studies examining the correlation of tramadol poisoning and its blood concentration proved that seizures are dependent on dose of tramadol but is independent on blood concentration of tramadol, age, sex and history of addiction.(22) As in this case most of the reported cases of tramadol induced seizures are of generalized tonic clonic type and occurs within 24 hours of tramadol consumption. (23)

### Conclusion:

The seizure inducing effect of tramadol is widely studied. The tramadol can provoke seizure in patients with epilepsy and those with no history of epilepsy even with the recommended doses. The other precipitating factors are excessive doses or co-administration with other seizure inducing drugs. Along with these established adverse events, the tramadol is exhibiting its wonder by providing great relief in pain.

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